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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,620	06/27/2007	Jonni Moore	P-7671-US	5253

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EXAMINER	
MARTIN, PAUL C	

ART UNIT	PAPER NUMBER
1657	

NOTIFICATION DATE	DELIVERY MODE
01/05/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTO@pczlaw.com
Arch-USPTO@pczlaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/594,620	MOORE ET AL.	
	Examiner	Art Unit	
	PAUL C. MARTIN	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,9-12 and 14-28* is/are pending in the application.

4a) Of the above claim(s) *14-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,9-12 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3, 9-12 and 14-28 are pending in this application, Claims 14-27 are acknowledged as withdrawn, Claims 1, 3, 9-12 and 28 were examined on their merits.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/10/2010 has been entered.

The rejection of Claims 1, 3 and 9-12 under 35 U.S.C. § 103(a) as being unpatentable over Fontenot *et al.* (2003) has been withdrawn due to the Applicant's amendments to the claims filed 12/10/2010.

Response to Amendment

The Declaration under 37 CFR 1.132 filed 12/10/2010 is sufficient to overcome the rejection of claims 1, 3 and 9-12 based upon Fontenot *et al.* (2003), as the Examiner is persuaded that Fontenot *et al.* does not use both CFSE and a viability marker to measure the proliferation of CD3/$CD4^+$ T-cells.

Response to Arguments

Applicant's arguments, see Remarks, filed 12/10/2010, with respect to the rejection(s) of claim(s) 1, 3, 6, 7 and 9-12 under 35 U.S.C. § 103(a) have been fully considered and are persuasive as the Examiner is persuaded that Fontenot *et al.* does not use both CFSE and a viability marker to measure the proliferation of CD3/$CD4^+$ T-cells. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Shapiro (2003).

Claim Objections

Claims 6, 7, 8 and 13 are objected to because of the following informalities: The text of all canceled claims should be deleted from the claims listing. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 9-12 and 28 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Fontenot *et al.* (2003) in view of Shapiro (2003).

Fontenot *et al.* teaches a method wherein peripheral blood mononuclear cells (PBMCs) and bronchoalveolar lavage (BAL) cells are obtained from subjects diagnosed with chronic beryllium disease (CBD) are stained with cell surface markers; monoclonal antibodies to CD4, CD8 and CD28 in order to identify the lymphocyte (T-cell) population (Pg. 777, Column 1, Lines 15-34 and Column 2, Lines 25-27); contacting the identified BAL T-cell subpopulation with the intracellular protein stain CFSE (Pg. 777, Column 1, Lines 36-37); contacting the BAL $CD4^+$ T-cells with 100 µM Beryllium sulfate ($BeSO_4$); and measuring the loss of in fluorescence intensity indicative of proliferation and CBD subject sensitivity to beryllium (Pg. 781, Fig. 7A) and wherein a confirming thymidine incorporation proliferation assay also showed increased proliferation in sorted $CD4^+$ cells from a CBD subject, which were exposed to 100 µM $BeSO_4$ as compared to control indicative of sensitivity to beryllium in the CBD subject (Pg. 781, Fig. 7B) and wherein both PBMC and BAL T-cells from CBD subjects are used in beryllium exposure experiments (Pg. 780, Fig. 5).

Fontenot *et al.* does not teach a method wherein peripheral blood leukocytes (PBL) are used with CFSE in a beryllium sensitivity assay or wherein the step of selecting a subpopulation of said PBL using a cell surface marker and a viability marker wherein the viability marker enables the exclusion of dead cells that lose CFSE; or wherein the viability marker is TO-PRO-3™.

Shapiro teaches the monitoring of cellular proliferation of $CD4^+$ lymphocytes as indicated by dilution of CFSE wherein TO-PRO-3™ was used to exclude dead cells (Pg. 373, Fig. 7-24).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Fontenot *et al.* wherein BAL T-Cells are stained with CFSE in order to measure proliferation due to exposure to beryllium by substituting PBL T-cells for BAL cells because the reference teaches the use of both types of cells in beryllium exposure assays and one of ordinary skill in the art would have recognized that the cell types were art-recognized equivalents. The MPEP states:

> In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. *In re Ruff,* 256 F.2d 590, 118 USPQ 340 (CCPA 1958)

One of ordinary skill in the art would have been motivated to make this substitution because the inherent advantages of using blood derived lymphocytes as opposed to BAL derived lymphocytes. Obtaining blood lymphocytes only requires a simple draw blood from a subject whereas BAL is a medical procedure requiring passing a bronchoscope through the mouth or nose of a subject and into the lung. There would have been a reasonable expectation of success in making this substitution as the reference teaches the use of both types of lymphocytes. It would have been further obvious to one of ordinary skill in the art at the time of the invention to modify the method of Fontenot *et al.* for monitoring the cellular proliferation of a cell marker selected subpopulation ($CD4^+$) PBL cells using CFSE to include the use of the viability marker TO-PRO-3™ as taught by Shapiro because the use of the viability stain would enable the researcher to selectively mark and exclude dead cells from the assay. One of ordinary skill in the art would have been motivated to make this modification because the exclusion of dead cells would have been desirable in an assay of cellular proliferation in live cells. There would have been a reasonable expectation of success in making this modification because both methods are drawn to assays of cellular proliferation using CFSE and $CD4^+$ cells.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL C. MARTIN whose telephone number is (571)272-3348. The examiner can normally be reached on M-F 12pm-8pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1657

12/29/2010

/JON P WEBER/
Supervisory Patent Examiner, Art Unit 1657